

**REMARKS**

**Status Summary**

Claims 1-27, 30-33, and 37-40 were canceled previously. Claims 28, 29, 34-36, and 41-59, are pending. Claims 42, 44-51, and 53-59 are withdrawn as being directed to a non-elected invention. Claims 28, 29, 34-36, 43, and 52 are rejected under U.S.C. §112, second paragraph, as allegedly indefinite. Claims 28, 29, 34-36, 43, and 52 are rejected under 35 U.S.C. §112, first paragraph, as allegedly non-enabling. Given that claim 41 is neither rejected nor withdrawn, it is understood that claim 41 is in condition for allowance.

Applicants also wish to clarify that the outstanding official action appears to have been improperly issued as a final rejection given that the prior non-final official action mailed 14 September 2006 considered canceled the original claims on the merits, which were canceled on the same date as the filing date. A response to the official action mailed 14 September 2006 was not submitted. Rather, a second requirement for restriction of claims was mailed 27 February 2007, noting the error in prior consideration of canceled claims. Accordingly, the official action mailed 23 January 2008 was the first official action considering pending claims on the merits. On 7 February 2008, a final rejection was mailed, stating that the immediately preceding action was improperly designated a non-final rejection. Applicants disagree, again noting that the official action mailed 23 January 2008 was the first official action considering pending claims on the merits.

Responsibility for this application was transferred to present counsel shortly before expiration of the statutory period for responding to the official action mailed 7 February 2008. To allow additional time for consideration of how to proceed, a notice of appeal was filed 7 August 2008. Notwithstanding filing of the notice of appeal, it is maintained that the official action mailed 7 February 2008 was an improper final rejection.

Claims 28 and 35 are amended herein. Reconsideration in view of the following remarks and amendments is respectfully requested.

**Rejection Under 35 U.S.C. §112, Second Paragraph**

Claims 28, 29, 34-36, 43, and 52, are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite because the claims specify “at a position corresponding to.”

The examiner states that the correspondence between the specified substitutions in SEQ ID NO: 12 and the sites within any other protox protein is unclear. Official action, page 2.

Independent claims 28 and 35 are amended to specify “at a position corresponding to position 221, 226, 227, 369, 371, 432, 436, 481, or 517 of SEQ ID NO: 12 *as set forth in the alignment shown in Table 1.*” Support for this amendment is found in Table 1, page 120 in the specification as originally filed. A skilled artisan recognizes from Table 1 those amino acid residues that correspond to the designated positions in SEQ ID NO: 12. Accordingly, the claims are not indefinite and the applicants respectfully request the rejection be withdrawn.

*Rejection Under 35 U.S.C. §112, First Paragraph*

Claims 28, 29, 34-36, 43, and 52 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Specifically, the examiner states that the instant application enables the transformation of a plastome of a tobacco plant with a mutation at position 226 of SEQ ID NO: 12, but fails to enable the plastome transformation in any plant other than tobacco. Official action, page 3. In support of this contention, the examiner cites Lutz *et al.*, *Plant Physiology*, 2007, 145: 1201-1210 and Kanevski *et al.*, *Plant Physiology*, 1999, 119: 133-141. The examiner relies on Lutz as teaching that, at the time of the instant invention, plastome transformation was routine only in tobacco. Official action, pages 5-6. The examiner relies on Kanevski *et al.*, *Plant Physiology*, 1999, 119: 133-141 as teaching obstacles in plastome transformation. In particular, Kanevski discloses that plastome transformation of sunflower with a *Synechococcus* gene did not result in protein production, possibly due to incompatibility at the level of translation or an inability of the protein to assemble using the indigenous folding machinery. Official action, page 6.

As a matter of Patent Office practice, the burden rests upon the Patent Office to establish a *prima facie* case of a failure to comply with 35 U.S.C. § 112, first paragraph, with respect to the invention described and claimed in applicants' presumptively enabling patent application. *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 169 USPQ 367 (C.C.P.A. 1971). Applicants respond that a *prima facie* case of lack of enablement has not been made.

The legal standard for enablement is whether one reasonably skilled in the art could make and use the invention based on the disclosure of the application and knowledge in the art without undue experimentation. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). Enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly excessive." *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996). In *Johns Hopkins Univ. v. CellPro*, 152 F.3d 1342 (C.A.Fed. (Del.) 1998), the Court of Appeals for the Federal Circuit rejected appellants' argument that methods for producing CD24 antibodies were generally "more difficult" than other monoclonal antibodies as sufficient to show lack of enablement.

The examiner has failed to make a *prima facie* case of lack of enablement in that, based on the disclosure of the instant application, a skilled artisan could readily transform plastomes of plants other than tobacco with nucleic acids encoding protox enzymes, as set forth in the claims, using the routine techniques.

The instant application teaches plastome transformation of a wide range of monocot and dicot species with chimeric genes that express modified protox enzymes, such as those described in the instant claims. For example, the specification teaches that plastome transformation can be achieved by (1) introducing the modified protox gene into a plastome of a cell, which is operatively linked to a promoter capable of inducing expression in both green and non-green chloroplasts, (2) expressing the encoded enzyme in the plastids of the plant cells and (3) selecting a cell that is resistant to a herbicidal compound that naturally inhibits the activity of the enzyme, whereby the resistant cell comprises transformed plastomes (*see, e.g.* page 70, lines 15-20). The inventors further provide examples of promoters that may be used to express the modified protox enzymes, plastome transformation vectors and examples of herbicides that may be used as selective agents (*see, e.g.*, pages 66-67, bridging paragraph, pages 66-67, bridging paragraph, pages 59-66, page 68, lines 23-26).

Still further, the instant application acknowledges the importance of employing appropriate selectable markers (*see* pages 70-71, bridging paragraph). In particular, it is described that antibiotic resistant markers may be ineffective markers for plant transformation. For example, natural spectinomycin and streptomycin resistance in maize obviate the use of the bacterial *aadA* gene, since expression of this gene also results in spectinomycin or streptomycin resistance. The instant application teaches that preferred selectable markers for plastome transformation include (1) markers that are selectively transcribed in plastids but not in nucleus, (2) markers that are not dependent on photosynthetic competence or the presence of fully differentiated chloroplasts, and (3) markers having a level of resistance that is dependent on an adjustable external parameter, such as light (*see* page 72, lines 3-9). For example, chimeric genes are useful selectable markers for plastome transformation, including for example, mutated EPSP synthase genes, or mutated ALS genes fused to a promoter capable of expression in plant plastids to select transplastomic plant cells using various herbicides (see e.g., pages 69-70).

With respect to Lutz, applicants submit that the examiner has relied upon an abbreviated sentence of the cited document, which is therein over-interpreted and taken out of context. Lutz states that “[p]lastid transformation is routine only in tobacco,” citing art from 1990 and 1993, which is well before the priority date of the instant application. In the *very same sentence*, Lutz adds that this technique has “rapidly expanded to diverse crops,” including potato, tomato, lettuce, soybean, cotton, cauliflower, and poplar, in each case citing original and peer-reviewed journal publications demonstrating plastome transformation in the respective plants. Accordingly, applicants expressly disagree that the cited text of Kavenski, accurately reflects that one of skill in the art would be unable, following a review of the instant application, to achieve plastome transformation as presently claimed. Rather, when taken in context, Kavenski summarizes that one of skill in the art could readily accomplish plastome transformation in many plants, and therefore, including the inventive transformation of sequences as set forth in the pending claims.

In further support that plastome transformation techniques were available for use in plants other than tobacco, numerous patents describe relevant methods for plastome transformation, which patents are presumed valid under 35 U.S.C. § 282. For example, U.S. Patent No. 5,451,513 includes claims directed to methods for obtaining stably plastid-

transformed cells of a multicellular plant, which claims are not otherwise limited to any particular plant; U.S. Patent No. 5,545,817 claims methods for producing a peptide of interest in a solanaceous plant cell by plastid expression in the cell; U.S. Patent No. 5,545,818 claims methods for enhancing the expression of an insecticidal *Bacillus thuringiensis* toxin in a plant cell by plastid expression of the toxin in plants, including cotton; and U.S. Patent No. 5,576,198 claims methods of providing for transcription of a DNA sequence of interest in a plant plastid organelle using an expression construct, and further describes use of such methods in potato, corn, flowers such as petunia, rose, and carnation, fruits, such as tomato, and oilseed crops such as *Brassica*, soybean, corn, safflower, or sunflower.

With respect to Kanevski, applicants initially note that this study describes replacing the *rbcL* gene in tobacco plants with a plastid DNA containing the *rbcL* gene from either sunflower or *Synechococcus*, along with the selectable marker *aadA*. Kanevski reports that tobacco transformants containing the *rbcL* gene produced mRNA, however, the encoded protein was not detected. Accordingly, such findings do not address the question regarding the amount of experimentation required to transform plastomes in *non-tobacco* plants, as questioned by the examiner. The examiner acknowledges that the instant application enables plastome transformation in tobacco, and therefore, Kanevski does nothing to support the basis for rejection.

Based upon the foregoing, neither Lutz nor Kavenski establish that plastome transformation in plants other than tobacco was not accomplished by routine techniques as of the priority date of the instant application. Absent such support or a well-reasoned argument as to the same, a *prima facie* case of lack of enablement has not been made. Accordingly, withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

*Voluntary Amendment*

Claim 35 is amended to correct a minor typographical error. Specifically, the spelling of the term protoporphyrinogen is corrected.

**CONCLUSION**

Entry of the foregoing amendments is respectfully requested. Should any questions arise regarding the amendment, the examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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